

the United States (up to 1 million people). This form of diabetes usually strikes children and young adults, who need several insulin injections a day or an insulin pump to survive. Insulin, although critical for controlling blood glucose, is no cure. Most people with type 1 diabetes eventually develop one or more complications, including damage to the heart and blood vessels, eyes, nerves, and kidneys.

In islet transplant, islets are extracted from the pancreas of a deceased donor and infused into a person with difficult-to-control type 1 diabetes through the portal vein of the liver. In successful transplants, the cells lodge in the liver's small blood vessels and begin producing insulin.

In the 1990s, islet transplant rarely succeeded in freeing patients from insulin injections for more than a year. In June 2000, however, a research team led by Dr. James Shapiro at the University of Alberta in Edmonton, Canada, reported sustained insulin independence in seven patients transplanted with islets from two to four donor pancreases. The patients received an immunosuppressive regimen that omitted glucocorticoids, also known as corticosteroids, which were often used to prevent rejection but are now thought to be toxic to islets. In the next few years, researchers participating in the Immune Tolerance Network, a collaboration of clinical and basic researchers sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and the Juvenile Diabetes Research Foundation Interna-

tional, replicated what became known as the Edmonton protocol.

Despite these gains, scientists continue to grapple with several impediments to the wider testing of islet transplant. One is the scarcity of islets. Only about 6,000 donor pancreases become available each year, and many are used for whole-organ transplant. Posing another obstacle are the potentially serious side effects, such as anemia, nerve damage, meningitis, and vulnerability to infection from immunosuppressives. Finally, in some transplanted patients, donor islets function well initially, but, in time, diabetes recurs. Why the islets die is not well understood.

Researchers in the newly funded centers will be designing studies to improve the isolation and viability of islets, reduce the complications of the transplant procedure (eg, bleeding and clotting), reduce the side effects of immunosuppression, trace the fate of islets after transplant and determine why donor islets sometimes fail, and evaluate new ways to safely prevent immune rejection of donor tissues.

Newly designed studies will be submitted for review by the US Food and Drug Administration, the NIDDK/NIAID Islet Transplantation Data and Safety Monitoring Board, and local institutional review boards before being offered to patients. Patient enrolment is scheduled to begin in 2005.

The consortium consists of the following principal investigators and centers: Dr. William Clarke, University of Iowa (Data Coordinating Center), Iowa City, Iowa; Dr. Camillo Ricordi, University of Miami, Miami, Florida; Dr. Bernhard Hering, University of Minnesota,

Minneapolis, Minnesota; Dr. Ali Naji, University of Pennsylvania, Philadelphia, Pennsylvania; Dr. James Shapiro, University of Alberta, Edmonton; and Dr. Olle Korsgren, Uppsala University, Uppsala.

The consortium is supported by a special funding program for type 1 diabetes research, which provides a total of \$1.14 billion from fiscal year 1998 through fiscal year 2008 to supplement other funds for type 1 diabetes research made available through the regular NIH appropriations process.

Other NIH-funded initiatives are also fostering progress in islet transplant. The Collaborative Islet Transplant Registry (<http://www.nih.gov/news/pr/sep2004/niddk-07.htm>), which recently published its first annual report, collects, analyzes, and disseminates data on islet transplants performed in the United States and Canada. Ten Islet Cell Resource Centers (<http://www.ncrr.nih.gov/clinical/cricr.asp>) harvest, purify, and ship islets for transplant and research. The Immune Tolerance Network (www.immunetolerance.org) is an international consortium dedicated to evaluating new treatments for autoimmune diseases, asthma, and allergic diseases and to preventing the rejection of transplanted organs and islets. The Beta Cell Biology Consortium (www.betacell.org) facilitates interdisciplinary efforts to understand islet development and function. The Non-Human Primate Islet Transplantation Consortium develops and tests new protocols for immune suppression in transplant recipients before these protocols are tested in patients.

NIAID Forms Clinical Consortium to Improve Success of Organ Transplants

The National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health (NIH), launched a three-site consortium spanning Boston, Cleveland, and Philadelphia that will work to improve the outcomes of organ transplant. Although organ replacement prolongs survival for people suf-

fering from end-stage organ failure, it rarely restores normal life expectancy and can sometimes lead to health problems associated with long-term use of immunosuppressive drugs, which reduce the risk of transplant rejection but also weaken the immune system against disease.

The consortium will also receive support from two other NIH components, the National Institute of Diabetes and Digestive and Kidney Diseases and the National Heart, Lung, and Blood Institute. Funding for the three 5-year grants totals an estimated \$43 million.

More than 25,000 organ transplants were performed in the United States in 2003, according to the Organ Procurement and Transplantation Network. As of August 2004, more than 86,000 people have their names on waiting lists for organs such as hearts, lungs, kidneys, and intestines.

Obstacles to successful organ replacement include genetic incompatibility between donor and recipient and transplant rejection by the recipient's immune system. Also, patients who

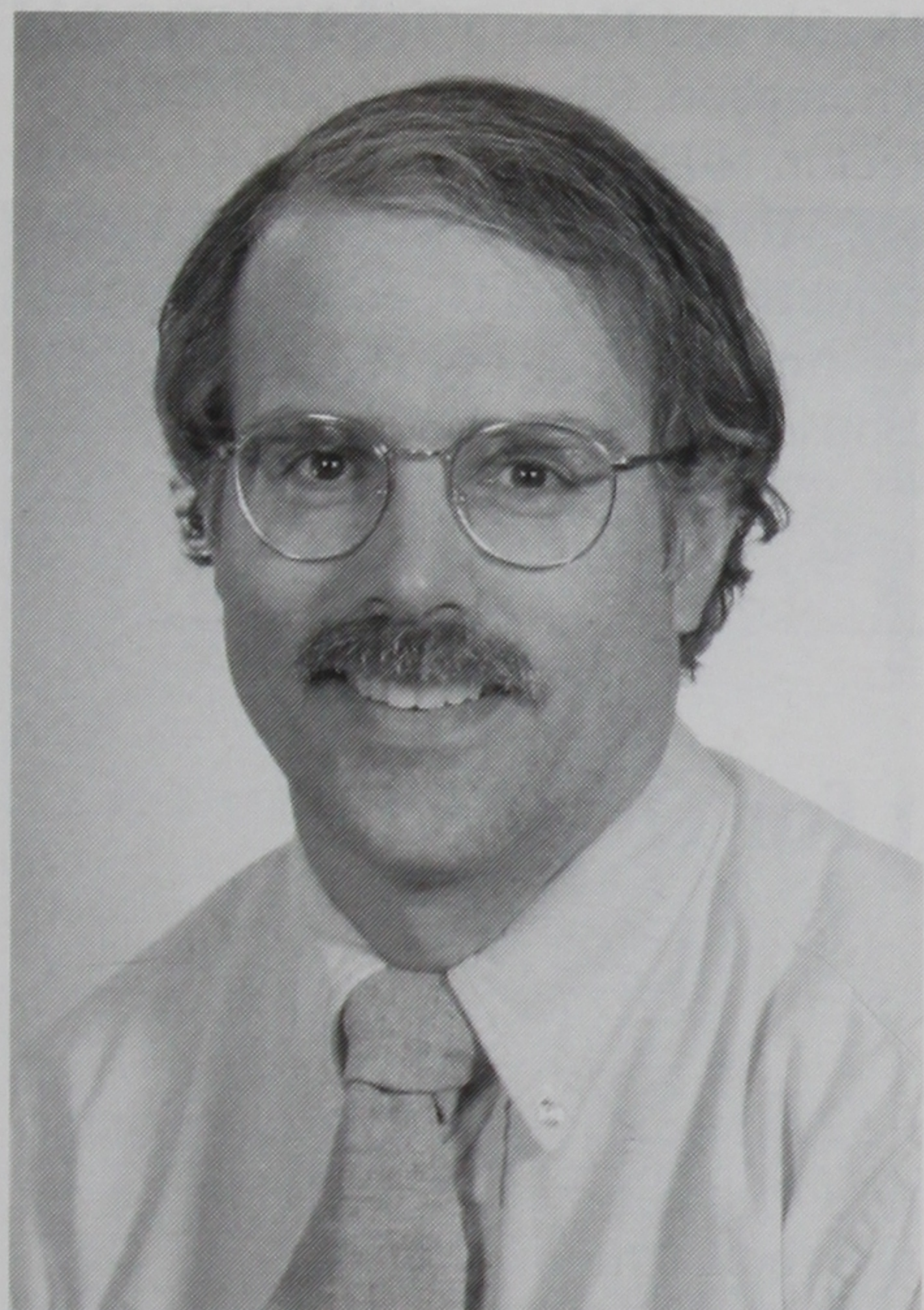
take immunosuppressive drugs for a long period of time are more susceptible to conditions such as diabetes, high blood pressure, and loss of kidney function.

The consortium will seek to identify genetic factors in patients that could help doctors predict transplant outcomes and responses to post-transplant therapy, develop diagnostic tests that enable early detection and ongoing monitoring of immune-related processes, and test the safety and ef-

fectiveness of new, less toxic immunosuppressive drugs.

The three institutions in the consortium and the principal investigator at each are Brigham and Women's Hospital, Boston, Mohamed H. Sayegh, MD; Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Peter Heeger, MD; and University of Pennsylvania, Philadelphia, Abraham Shaked, MD, PhD.

University of Iowa Presents Award for Distinguished Mentoring



Jeffrey C. Murray

Jeffrey C. Murray, MD, professor of pediatrics in the University of Iowa (UI) Roy J. and Lucille A. Carver College of Medicine, has been named the recipient of the college's third annual Award for Distinguished Mentoring. Murray received the award during a ceremony and lecture on September 29, 2004.

Mary-Claire King, PhD, American Cancer Society Professor and professor of genome sciences and medicine (medical genetics) at the University of Washington, delivered the third annual

Distinguished Mentor's Lecture, titled "Race, Genes, and Medicine."

The Distinguished Mentoring Award honors UI Carver College of Medicine faculty members whose careers have emphasized the mentoring of students, postdoctoral research fellows, and faculty who have forged their own notable careers. The Distinguished Mentor's Lecture highlights the award for mentoring by bringing to the UI world-class scientists who embody the ideals of the award and its recipient. The award was initially established and is supported by a gift to the UI Foundation from UI graduates Nancy and Daryl Granner, MD, of North Liberty, Iowa.

A UI faculty member since 1984, Murray is widely regarded as an outstanding clinician, researcher, and teacher. His clinical activities center on newborn medicine and care of children born with birth defects. His research incorporates genetics, molecular biology, embryology, and epidemiology to study birth defects, particularly cleft lip and palate. He has been active in a variety of international studies to provide improved treatment and prevention for birth defects.

Recently, researchers from eight countries, led by Murray's UI research team, reported identifying a genetic variation that increases the risk of a baby being born with a cleft lip and palate. The finding helps explain 10 to

15% of all cases of the common form of cleft lip and palate and offers new directions for predicting, preventing, and treating the condition.

Graduate students and postdoctoral fellows in Murray's laboratory take on leadership roles in research studies and assume primary responsibility for project design and implementation. In the recent cleft lip and palate finding, Theresa Zuccherro, a doctoral student in the UI Interdisciplinary Program in Genetics, played a key role in getting the project under way and helped organize deoxyribonucleic acid (DNA) testing of thousands of study participants—a major collaborative effort among multiple laboratories in Asia, Europe, and South America. UI undergraduate students also work in Murray's laboratory.

King, who delivered the Distinguished Mentor's Lecture, is internationally recognized as a groundbreaking researcher and an advocate for using science to advance human rights. She is perhaps best known for her 1990 discovery that mutations in a single gene, today known as *BRCA1*, cause breast cancer in certain high-risk families. King's finding was a watershed moment in genetics research and has been emulated by scientists studying other serious illnesses, such as Alzheimer's disease, Parkinson's disease, and prostate cancer.